

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 80248/WO	FOR FURTHER ACTION <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. PCT/EP 00/ 01798	International filing date (day/month/year) 02/03/2000	(Earliest) Priority Date (day/month/year) 11/03/1999
Applicant SOCIETE DES PRODUITS NESTLE S.A. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

LACTOBACILLUS STRAINS CAPABLE OF PREVENTING DIARRHOEA CAUSED BY PATHOGENIC BACTERIA AND ROTAVIRUSES

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

/EP 00/01798

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K35/74 C12N1/20 A23L1/29 A23C9/152 //(C12N1/20, C12R1:225)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 577 903 A (NESTLE SA) 12 January 1994 (1994-01-12) cited in the application the whole document ---	1,2,7-13
X	WO 98 06411 A (DICOFARM SPA ; GUANDALINI STEFANO (IT)) 19 February 1998 (1998-02-19) the whole document ---	1-13
X	US 5 837 238 A (MOLLSTAM BO ET AL) 17 November 1998 (1998-11-17) the whole document --- -/--	1-3,7-13

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

5 June 2000

Date of mailing of the international search report

13/06/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Fernandez y Branas, F

INTERNATIONAL SEARCH REPORT

International Application No

EP 00/01798

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KAILA M ET AL: "VIABLE VERSUS INACTIVATED LACTOBACILLUS STRAIN GG IN ACUTE ROTAVIRUS DIARRHOEA" ARCHIVES OF DISEASE IN CHILDHOOD, vol. 72, no. 1, 1 January 1995 (1995-01-01), pages 51-53, XP002058045 the whole document ---	1-4,7-13
X	EP 0 861 905 A (PROGE FARM S R L) 2 September 1998 (1998-09-02) page 4, line 25 -page 5, line 35 ---	1-13
X	WO 95 33046 A (BRACCO SPA ;DIBRA SPA (IT); MORELLI LORENZO (IT); BOTTAZZI VITTORI) 7 December 1995 (1995-12-07) page 9 -page 12 page 13 -page 27 ---	1-13
X	TUOMOLA E.M. ET AL: "Adhesion of some probiotic and dairy Lactobacillus strains to Caco-2 cell cultures" INTERNATIONAL JOURNAL OF FOOD MICROBIOLOGY, vol. 41, 1998, pages 45-51, XP002115137 the whole document ---	1-13
X,P	WO 99 29833 A (FONDEN RANGNE ;SVENSSON ULLA (SE); ALELJUNG PER (SE); ARLA EKONOMI) 17 June 1999 (1999-06-17) the whole document ---	1-5,7-13
X	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US PRASAD, JAYA ET AL: "Selection and characterisation of Lactobacillus and Bifidobacterium strains for use as probiotics." retrieved from STN XP002121832 abstract & INTERNATIONAL DAIRY JOURNAL, (1998) VOL. 8, NO. 12, PP. 993-1002., ---	1-4
X	MAJAMAA H ET AL: "LACTIC ACID BACTERIA IN THE TREATMENT OF ACUTE ROTAVIRUS GASTROENTERITIS" JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION,US,RAVEN PRESS, NEW YORK, NY, vol. 20, no. 3, 1 April 1995 (1995-04-01), pages 333-338, XP002058047 ISSN: 0277-2116 the whole document ---	1-4,6-13

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INTERNATIONAL SEARCH REPORT

International Application No

T/EP 00/01798

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MIETTINEN, MINJA (1) ET AL: "Lactobacilli and streptococci induce interleukin-12 (IL-12), IL-18, and gamma interferon production in human peripheral blood mononuclear cells."</p> <p>INFECTION AND IMMUNITY, (DEC., 1998) VOL. 66, NO. 12, PP. 6058-6062., XP002121831</p> <p>the whole document</p> <p>-----</p>	1-13

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

EP 00/01798

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0577903	A	12-01-1994	AT 161181 T	15-01-1998
			AU 4158893 A	13-01-1994
			CA 2099855 A	07-01-1994
			CZ 9301342 A	19-01-1994
			DE 69223615 D	29-01-1998
			DE 69223615 T	09-04-1998
			DK 577903 T	06-04-1998
			ES 2111625 T	16-03-1998
			FI 933001 A	07-01-1994
			GR 3025971 T	30-04-1998
			HU 66632 A	28-12-1994
			JP 2672247 B	05-11-1997
			JP 6098782 A	12-04-1994
			NO 932407 A	07-01-1994
			NZ 248056 A	28-08-1995
			PL 299543 A	21-02-1994
			SK 71193 A	08-06-1994
			US 5578302 A	26-11-1996
WO 9806411	A	19-02-1998	IT RM960571 A	09-02-1998
			AU 3863997 A	06-03-1998
			EP 0918531 A	02-06-1999
US 5837238	A	17-11-1998	AU 3154897 A	05-01-1998
			EP 0923293 A	23-06-1999
			PL 330324 A	10-05-1999
			WO 9746104 A	11-12-1997
EP 0861905	A	02-09-1998	IT MI970426 A	27-08-1998
WO 9533046	A	07-12-1995	IT 1269838 B	15-04-1997
			IT 1274733 B	24-07-1997
			AT 163042 T	15-02-1998
			AU 686389 B	05-02-1998
			AU 2613995 A	21-12-1995
			BR 9507752 A	07-10-1997
			DE 69501591 D	12-03-1998
			DE 69501591 T	10-06-1998
			DE 760848 T	28-08-1997
			EP 0760848 A	12-03-1997
			ES 2099056 T	16-05-1997
			FI 964681 A	08-01-1997
			GR 97300016 T	31-05-1997
			GR 3026758 T	31-07-1998
			HU 75555 A	28-05-1997
			JP 10500577 T	20-01-1998
			NO 964966 A	23-01-1997
			NZ 287420 A	19-12-1997
			US 5709857 A	20-01-1998
WO 9929833	A	17-06-1999	SE 510813 C	28-06-1999
			AU 1896899 A	28-06-1999
			SE 9704577 A	09-06-1999

PATENT COOPERATION TREATY

BOVARIASTRASSE 7 · 80336 MÜNCHEN

29. März 2001

WV: / LF:

PCT

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

STRAUS, Alexander
BECKER, KURIG, STRAUS
Bavariastrasse 7
D-80336 München
ALLEMAGNE

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Rule 71.1)

Date of mailing
(day/month/year) 28.03.2001

Applicant's or agent's file reference
80248/WO

IMPORTANT NOTIFICATION

International application No.
PCT/EP00/01798

International filing date (day/month/year)
02/03/2000

Priority date (day/month/year)
11/03/1999

Applicant
SOCIETE DES PRODUITS NESTLE S.A. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Hundt, D

Tel. +49 89 2399-8042



Applicant's or agent's file reference	248/H0	International application.	PCT/PCC/C1798
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**INDICATIONS RELATING TO DEPOSITED MICROORGANISM
OR OTHER BIOLOGICAL MATERIAL**

(PCT Rule 13bis)

A. The indications made below relate to the deposited microorganism or other biological material referred to in the description on page 3, line 30, page 5, line 8, page 7, line 12, page 22, line 22	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution CNCM Collection Nationale de Cultures de Microorganismes	
Address of depositary institution (including postal code and country) Institut Pasteur 28, Rue du Docteur Roux F-75724 Paris Cedex 15	
Date of deposit 12.01.1999	Accession Number I-2116
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input checked="" type="checkbox"/> This sheet was received by the International Bureau on: 22 MAY 2000
Authorized officer	Authorized officer Gauri

TRAITÉ DE BUDAPEST SUR LA RECONNAISSANCE
INTERNATIONALE DU DÉPÔT DES MICRO-ORGANISMES
AUX FINS DE LA PROCÉDURE EN MATIÈRE DE BREVETS

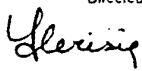
FORMULE INTERNATIONALE

DESTINATAIRE :

RECEPISSE EN CAS DE DÉPÔT INITIAL,
délivré en vertu de la règle 7.1 par
l'AUTORITÉ DE DÉPÔT INTERNATIONALE
identifiée au bas de cette page

SOCIÉTÉ DES PRODUITS NESTLÉ S.A.
Patents department
Avenue Nestlé 55
CH-1800 Vevey

NOM ET ADRESSE
DU DÉPOSANT

I. IDENTIFICATION DU MICRO-ORGANISME	
Référence d'identification donnée par le DÉPOSANT :	Numéro d'ordre attribué par l'AUTORITÉ DE DÉPÔT INTERNATIONALE :
NCC 2461	I - 2116
II. DESCRIPTION SCIENTIFIQUE ET/OU DESIGNATION TAXONOMIQUE PROPOSÉE	
Le micro-organisme identifié sous chiffre I était accompagné :	
<input checked="" type="checkbox"/> d'une description scientifique <input checked="" type="checkbox"/> d'une désignation taxonomique proposée (Cocher ce qui convient)	
III. RECEPTION ET ACCEPTATION	
La présente autorité de dépôt internationale accepte le micro-organisme identifié sous chiffre I, qu'elle a reçu le 12 JANVIER 1999 (date du dépôt initial) ¹	
IV. RECEPTION D'UNE REQUÊTE EN CONVERSION	
La présente autorité de dépôt internationale a reçu le micro-organisme identifié sous chiffre I le (date du dépôt initial) et a reçu une requête en conversion du dépôt initial en dépôt conforme au Traité de Budapest le (date de réception de la requête en conversion)	
V. AUTORITÉ DE DÉPÔT INTERNATIONALE	
Nom : CNCM Collection Nationale de Cultures de Microorganismes Adresse : INSTITUT PASTEUR 28, Rue du Docteur Roux F-75724 PARIS CEDEX 15	Signature(s) de la (des) personne(s) compétente(s) pour représenter l'autorité de dépôt internationale ou de l'(des) employé(s) autorisé(s) : Mme Y. CERISIER Directeur Administratif de la CNCM  Date : Paris, le 12 février 1999

¹ En cas d'application de la règle 6.4.d), cette date est la date à laquelle le statut
d'autorité de dépôt internationale a été acquis.

Applicant's or agent's
file reference

80248/W0

International application No.

PCT/EP00/01798

INDICATIONS RELATING TO DEPOSITED MICROORGANISM
OR OTHER BIOLOGICAL MATERIAL

(PCT Rule 13bis)

A. The indications made below relate to the deposited microorganism or other biological material referred to in the description on page <u>3, line 30, page 5, line 8, page 7, line 12, page 22, line 22</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution CNCM Collection Nationale de Cultures de Microorganismes	
Address of depositary institution (including postal code and country) Institut Pasteur 28, Rue du Docteur Roux F-75724 Paris Cedex 15	
Date of deposit 12.01.1999	Accession Number I-2116
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	


<p>For receiving Office use only</p> <p><input type="checkbox"/> This sheet was received with the international application</p> <p>Authorized officer</p>	<p>For International Bureau use only</p> <p><input type="checkbox"/> This sheet was received by the International Bureau on:</p> <p>Authorized officer</p>
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 80248/WO		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP00/01798	International filing date (day/month/year) 02/03/2000	Priority date (day/month/year) 11/03/1999	
International Patent Classification (IPC) or national classification and IPC A61K35/74			
Applicant SOCIETE DES PRODUITS NESTLE S.A. et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 10 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input checked="" type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input checked="" type="checkbox"/> Certain documents cited VII <input checked="" type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 			
Date of submission of the demand 22/09/2000		Date of completion of this report 28.03.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Fayos, C Telephone No. +49 89 2399 2180	



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP00/01798

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

Description, pages:

1-21 as originally filed

Claims, No.:

1-13 as originally filed

Drawings, sheets:

1/9-9/9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP00/01798**

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

☐ copy of the earlier application whose priority has been claimed.

☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
see separate sheet

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 6
	No: Claims 1-5 and 7-13
Inventive step (IS)	Yes: Claims -
	No: Claims 1-13
Industrial applicability (IA)	Yes: Claims 1-13
	No: Claims -

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP00/01798

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item II

Priority

- 1- The priority date (11.03.1999) of the present application is valid.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 2- Reference is made to the following documents:

- D1: EP-A-0 577 903 (NESTLE SA) 12 January 1994 (1994-01-12) cited in the application
- D2: WO 98 06411 A (DICOFARM SPA ;GUANDALINI STEFANO (IT)) 19 February 1998 (1998-02-19)
- D3: US-A-5 837 238 (MOLLSTAM BO ET AL) 17 November 1998 (1998-11-17)
- D4: KAILA M ET AL: 'VIABLE VERSUS INACTIVATED LACTOBACILLUS STRAIN GG IN ACUTE ROTAVIRUS DIARRHOEA' ARCHIVES OF DISEASE IN CHILDHOOD, vol. 72, no. 1, 1 January 1995 (1995-01-01), pages 51-53, XP002058045
- D5: EP-A-0 861 905 (PROGE FARM S R L) 2 September 1998 (1998-09-02)
- D6: WO 95 33046 A (BRACCO SPA ;DIBRA SPA (IT); MORELLI LORENZO (IT); BOTTAZZI VITTORI) 7 December 1995 (1995-12-07)
- D7: TUOMOLA E.M. ET AL: 'Adhesion of some probiotic and dairy Lactobacillus strains to Caco-2 cell cultures' INTERNATIONAL JOURNAL OF FOOD MICROBIOLOGY, vol. 41, 1998, pages 45-51, XP002115137
- D8: see item VI below
- D9: DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US PRASAD, JAYA ET AL: 'Selection and characterisation of Lactobacillus and Bifidobacterium strains for use as probiotics.' retrieved from STN XP002121832 & INTERNATIONAL DAIRY JOURNAL, (1998) VOL. 8, NO. 12, PP. 993-1002.,
- D10: MIETTINEN, MINJA (1) ET AL: 'Lactobacilli and streptococci induce interleukin-12 (IL-12), IL-18, and gamma interferon production in human peripheral blood

mononuclear cells.' INFECTION AND IMMUNITY, (DEC., 1998) VOL. 66, NO. 12, PP. 6058-6062., XP002121831

D11: MAJAMAA H ET AL: 'LACTIC ACID BACTERIA IN THE TREATMENT OF ACUTE ROTAVIRUS GASTROENTERITIS' JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION, US, RAVEN PRESS, NEW YORK, NY, vol. 20, no. 3, 1 April 1995 (1995-04-01), pages 333-338, XP002058047 ISSN: 0277-2116

NOVELTY - Art. 33 (1) and (2) PCT

3- Claims 1-5 and 7-13 are not novel for the following reasons:

- Note:
- Claims 1-6 are product claims. A product (here a Lactic acid bacterium strain belonging to the genus *Lactobacillus*) is only defined by its components / elements and not by its intended use ("preventing colonization of the intestine with pathogenic bacteria causing diarrhoea and preventing infection of intestinal epithelial cells by rotaviruses"). Lactic acid bacterium strains belonging to the genus *Lactobacillus* are well known (see below), in particular *Lactobacillus rhamnosus* or *Lactobacillus paracasei*.
 - Claims 7-10 and 12-13 merely refer to the preparation of an ingestible support material containing the product of any of claims 1-6 (well known - see below).
 - Claim 11 refers to the use of a preparation according to any of claims 7-10 for the treatment and / or prophylaxis of disorders associated with diarrhoea (well known - see below).
 - "capable to grow in the presence of up to 0,4 % bile salts" is considered a parameter, by which a Lactic acid bacterium strain belonging to the genus *Lactobacillus* can be characterized, in this case.

3.1- D1 discloses (e. g. c. 1 lines 23-44) the use of an antigastritis

agent/strain/composition and/or anti ulcer agent/strain/composition capable of displacing pathogenic bacteria on intestinal and/or gastric cells and of adhering to intestinal cells. Said agent is produced (secreted in the culture medium) by a biologically pure culture of a Lactobacillus strain (Lactobacillus acidophilus CNCM I-1225) and is comprised in a support material such as milk, yogurt or milk based powders for therapeutic or prophylactic administration. [Note that gastritis and ulcer cause also diarrhoea and hence, the pathogenic bacteria that cause gastritis and ulcer cause also diarrhoea]

Therefore, claims 1-2, 7 and 9-13 are not novel in the light of D1.

- 3.2- D2 relates to the treatment of acute infant's diarrhoea (caused by e. g. rotavirus and pathogenic bacteria- p 5 line 16-20) using Lactobacillus GG (Lactobacillus casei subspecies rhamnosus) comprised in a rehydrating solution in amounts between 100,000 and 1,000,000 c.f.u. per 500 ml solution (see D2 claims). As mentioned on p 3 line 6 - p 4 line 15 the effect of Lactobacillus GG is achieved through an agent which is secreted by the bacteria.

Hence, D2 destroys the novelty of claims 1, 2, 4, 7 and 9, 11 and 12.

- 3.3- D3 discloses a method for treating diarrhea using one or more strains of Lactobacillus reuteri in amounts of e. g. 10^{10} - 10^{11} c.f.u. per g dose (c 4 lines 38-56) of a fluid of choice such as milk or yogurt (c 2 line 42). In particular, D3 (c 2 lines 63-67) shows the positive effect of Lactobacillus reuteri strain SD 2112 on recovery from acute diarrhea (75% rotavirus) through colonization of the gastrointestinal tract.

Therefore, in the light of D3, claims 1-2 and 7-13 lack novelty.

- 3.4- D5 discloses the use of Lactobacilli (belonging to the species Paracasei and Salivarius) capable of adhering to the cells of the intestinal mucosa and stable to bile juices (at least 0.4 %) for the manufacture of compositions (10^6 - $3 \cdot 10^9$ c.f.u. per unitary dose) such as milk and yogurt for the treatment of e. g. diarrhoea (p 4 line 24

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- p 6 line 35).

Therefore, in the light of D5, claims 1-5 and 7-13 are not novel.

3.5- D6 discloses (p 9-12) lactobacillus strains that have the ability to adhere to the human epithelial cells and are resistant to bile (p 26-27). The strains of D6 inhibit the growth of pathogens in the intestinal tract and are therefore useful for treatment and prophylaxis of diseases in which intestinal colonization by less favourable microorganisms occurs. These lactobacilli strains can also be employed in the manufacture of milk and related food products for the same purpose.

Hence, claims 1-2, 7 and 9-13 are not novel in the light of D6.

3.6- D7 relates to the investigation of the adhesion of several probiotic and dairy lactobacillus (such as *L. paracasei* - see e. g. table 1) strains to Caco-2 cell cultures and mentions that there evidence relating adhesion to the temporary colonization of human intestinal tract.

Thus, D7 destroys the novelty of claims 1-2, 4-5, 7 and 12.

3.7- *Lactobacillus paracasei* CNCM I-2116 (NCC 2461) appears to be formally novel over the cited prior art, since it is not strictly disclosed in any of the available prior art documents. Hence, claim 6 can be considered as being novel over the cited prior art.

INVENTIVE STEP - Art. 33 (1) and (3) PCT

4- Claims 1-5 and 7-13, which are not novel, cannot be considered as being inventive, and claim 6 lacks inventive step for the reasons stated below.

4.1- The closest prior art is represented by D5.

The closest prior art differs from the present application in that it does not explicitly mention *Lactobacillus paracasei* CNCM I-2116 (NCC2461)

The technical effect achieved in the present application is the prevention of colonization of the intestine with pathogenic bacteria causing diarrhoea and the prevention of infection of intestinal epithelial cells by rotaviruses, using *Lactobacillus paracasei* CNCM I-2116 (NCC 2461).

The objective problem posed in the present application is to provide additional bacterial strains that exhibit properties beneficial for man and / or animals.

The solution proposed is *Lactobacillus paracasei* CNCM I-2116 (NCC 2461).

Lactic acid bacterium strains belonging to the genus *Lactobacillus* such as *Lactobacillus rhamnosus* or *Lactobacillus paracasei* are known and have been used for therapeutical purposes.

4.2- The *Lactobacilli* of D5 have the following characteristics: stability to acids, stability to bile juices, capability of adhering to cells of the intestinal mucosa, and capability of producing only (or anyway in high prevalence) L(+) lactic acid (p 4-5). Furthermore, it is to be noted that *Lactobacilli* in general are catalase negative and gram positive and are either homofermentative (produce lactic acid) or heterofermentative (produce ethyl alcohol, CO₂, and often other acids in addition to lactic acid).

The *lactobacilli* of D5 are also isolated from human faeces (see e. g. p 3 line 23) and share typical structural and functional characteristics with the *Lactobacillus paracasei* strain of the present application, i. e. CNCM I-2116.

Since the present application does not provide any technical data concerning the isolation and characterization of *L. paracasei* CNCM I-2116 (see examples), which would differentiate it from the *lactobacilli* identified in D5, there is no reason to believe that *L. paracasei* CNCM I-2116 is functionally different from the strains of D5.

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4.3- The subject matter of claims 1-13 is therefore obvious in the light of the prior art cited in the search report.

Re Item VI

Certain documents cited

5- Certain published documents (Rule 70.10): D8

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 99/29833	17.06.99	08.12.98	08.12.97

Re Item VII

Certain defects in the international application

- 6- The relevant prior art should be identified in the description (Rule 5.1(1)(a)(ii) PCT).
- 7- It is not clear from the description of the present application that ST11 corresponds to the *L. casei* strain CNCM I-2116, since the specification therefor first appears on p 6 § 3 (Art. 5 PCT).

Re Item VIII

Certain observations on the international application

- 8- There appears to be an inconsistency between the claims (e. g. claims 4-6) and the description (e. g. p 6 § 3-4 among others) since the claims refer to *Lactobacillus paracasei* and the description refers to *lactobacillus casei*.

PATENT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
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in its capacity as elected Office

Date of mailing (day/month/year) 20 October 2000 (20.10.00)	
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Applicant RENIERO, Roberto et al	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

22 September 2000 (22.09.00)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

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